Diagnosis and Management of Opioid-Induced Bowel Dysfunction in Patients With Advanced Cancer

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Opioid-induced bowel dysfunction (OBD) is characterized by a constellation of symptoms, including constipation; dry, hard stools; straining; and incomplete evacuation. The use of a prophylactic bowel regimen that includes a stimulant laxative and stool softener generally is accepted and should be initiated at the start of opioid therapy. Effective prevention and treatment of OBD reduce the risk of associated physiologic complications and can improve pain management and quality of life for patients and their families.

Case Study

At age 27, Ms. J was newly diagnosed with stage IV gastric adenocarcinoma, with a gastric antrum tumor and extensive involvement of her lung, thoracic, abdominal, and pelvic lymph nodes, thoracic and lumbar vertebrae, and pelvic bones. She began a chemotherapy regimen of docetaxel, cisplatin, and 5-fluorouracil; an antiemetic regimen of aprepitant, dexamethasone, ondansetron, and lorazepam; and IV zoleodronic acid. Ms. J also began receiving oxycodone every four hours as needed for lower back pain. The toxicities of 5-fluorouracil and docetaxel include diarrhea; therefore, a prophylactic bowel regimen was deferred.

Ms. J returned to the clinic three weeks later for treatment, complaining of abdominal cramping, bloating, mild nausea, and anorexia, with decreased oral intake. She reported diarrhea for one week following chemotherapy; stools subsequently became small, hard, and difficult to pass. Prior to her cancer diagnosis, Ms. J moved her bowels once or twice daily. Although she was passing flatus, her last bowel movement was five days prior. Despite taking oxycodone at least five times daily, her persistent lower back pain had caused decreased physical activity. Ms. J feared that the new symptoms indicated her cancer was advancing.

Ms. J was afebrile, alert, and oriented. Her blood pressure was slightly decreased, with mild orthostatic changes. Oral mucosa and skin were slightly dry. Her abdomen was moderately distended, soft, and nontender, with hypoactive bowel sounds in all four quadrants. Bilateral lower extremity strength was 5 of 5, with normal deep tendon reflexes and sensation. Blood work revealed a white blood cell count of 1,700/mm³ and absolute neutrophil count of 500/mm³; therefore, digital rectal examination was deferred. Serum calcium was 9.5 mg/dl (within normal limits) when corrected for albumin. Creatinine and blood urea nitrogen were slightly elevated at 1.5 mg/dl and 20 mg/dl, respectively.

Diagnostic Evaluation

Although Ms. J’s assessment findings are consistent with OBD, other differential
diagnoses for her symptoms should be considered, given the extent of her disease and concomitant chemotherapy (see Figure 2). Persistent bowel sounds and flatus made gastric outlet obstruction and malignant bowel obstruction unlikely, and radiologic imaging of the abdomen was deferred. Normal neuromuscular findings made metastatic spinal cord compression unlikely; therefore, magnetic resonance imaging of the spine also was deferred. Laboratory findings ruled out hypercalcemia but, along with orthostasis, did indicate mild dehydration. Docetaxel and 5-fluorouracil are associated with diarrhea and, therefore, were not implicated. Although antiemetics such as the serotonin (5-HT₃) antagonist ondansetron can contribute to constipation, the time between scheduled doses and symptom onset made the association unlikely. Based on Ms. J’s symptom profile, recent opioid use, and exclusion of other etiologies, a diagnosis of OBD was established.

Opioid-Induced Bowel Dysfunction

Pathophysiology and Impact

The enteric nervous system is replete with opioid receptors, and opioid analgesics act as μ-opioid receptor agonists in the gastrointestinal tract (Neyens & Jackson, 2007). This inhibits gastric emptying and peristalsis, disrupts propulsion, and reduces secretion of water and electrolytes into the intestine, delaying transit (Holzer, 2009; Thomas, 2008). Those effects, combined with increased fluid reabsorption caused by prolonged contact of bowel contents with the intestinal mucosa, can produce profound constipation (Kurtz & Sessler, 2003), as well as other clinical manifestations of OBD.

Although opioid analgesics are extremely effective for the management of cancer-related pain, OBD is a common and debilitating side effect to which tolerance rarely develops (Chamberlain et al., 2009; Neyens & Jackson, 2007). OBD can cause serious complications, including fecal impaction, bowel obstruction or perforation, rectal tearing, hemorrhoids, and inadequate medication absorption (Larkin et al., 2008). Patients may decrease or terminate opioid therapy to facilitate defecation, resulting in inadequate pain control (Bell et al., 2009). OBD also can impair other quality-of-life domains, including participation in activities of daily living and emotional well-being (Bell et al., 2009; Kurtz & Sessler, 2003).

Assessment and Management

Despite the prevalence and clinical impact of OBD in patients with cancer, literature to date has focused primarily on the assessment and management of its most bothersome symptom, constipation (Bell et al., 2009). Prior to initiating opioids and at all subsequent encounters, assessment should be performed to determine bowel function and identify risk factors for constipation, including disease-related factors, medication use, fluid and dietary fiber intake, and physical activity. Bowel diaries can facilitate longitudinal evaluation of bowel function. Focused physical examination should include assessment of abdominal pain, firmness, distension, and bowel sounds. Patients with persistent constipation should be assessed for impaction, which is the presence of dry, hard stool in the rectum. Impaction can be identified by digital rectal examination; however, the examination is contraindicated in significantly myelosuppressed patients because of infection risk. Impaction should be treated as shown in Figure 3 (Woolery et al., 2008).

Although expert consensus supports the use of prophylactic bowel regimens in all patients taking opioids, a paucity of strong evidence demonstrates the efficacy of one regimen over another (Woolery et al., 2008). Cancer-specific guidelines recommend regimens including pharmacologic (see Figure 4) and nonpharmacologic measures, with the goals of maximizing stool volume, softening stool, and enhancing peristalsis (Thomas, 2008) to achieve one nonforced bowel movement every one to two days. Prophylactic pharmacologic regimens typically include a stimulant laxative plus stool softener (National Comprehensive Cancer Network [NCCN], 2010; Woolery et al., 2008). Those agents should be titrated to achieve goals or switched if ineffective. Bulk-forming laxatives increase stool volume but should be used with caution in patients with advanced cancer because they...
require adequate fluid intake and physical activity to prevent exacerbation of constipation (Woolery et al., 2008).

Rescue laxatives are critical with persistent constipation and should be added after stimulants have been optimized. Some experts advocate the addition of osmotics, although their use may be limited because of cramping, bloating, and flatus (Thomas, 2008). Lubricant laxatives are useful for patients reporting excessive straining, but long-term use may cause malabsorption of fat-soluble vitamins (Avila, 2004). Enemas and rectal suppositories should be avoided in myelo-suppressed patients because of increased risk for infection with rectal tissue damage (Woolery et al., 2008).

Although the interventions discussed previously focus on treating a resultant symptom of OBD, newer agents that target its pathophysiologic basis are being investigated. Peripherally selective µ-opioid antagonists such as methylnaltrexone are administered concurrently with opioids and are directed at maintaining gastrointestinal function without reversing analgesia (Chamberlain et al., 2009; Neyens & Jackson, 2007). If patients with advanced cancer with OBD derive inadequate benefit from laxatives, subcutaneous methylnaltrexone should be considered (NCCN, 2010). Other routes of administration are under investigation (Neyens & Jackson, 2007).

### Treatment

Ms. J’s chemotherapy was delayed because of neutropenia. The healthcare team educated her about opioid side effects and established a regimen with the goal of defecation each morning after breakfast. Ms. J was prescribed two senna plus two docusate sodium every evening (to be titrated up to three times daily, if needed), as well as lactulose for immediate and rescue laxation. The team encouraged Ms. J to keep a bowel diary to monitor the efficacy of those interventions. Nonpharmacologic interventions were reviewed (e.g., adequate fluid and dietary fiber intake, exercise if appropriate, quiet and private environment for defecation, bowel diary [Woolery et al., 2008]). Ms. J’s analgesic regimen was modified to OxyContin® (Purdue Pharma), with oxycodone for breakthrough pain.

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**Figure 3. Prevention and Management of Constipation in Opioid-Induced Bowel Dysfunction**

*Note. Based on information from National Comprehensive Cancer Network, 2010; Woolery et al., 2008.*
Bulk Forming
• Methylcellulose (Citruce®, GlaxoSmithKline)
• Psyllium (Metamucil®, Procter & Gamble; Konsole®, Konsole Pharmaceuticals)
• Calcium polycarphil (Konsole® Fiber, Konsole Pharmaceuticals; Fibercon®, Wyeth; Perdiem Fiber Therapy®, Novartis AG)

Lubricant
• Mineral oil
• Mineral oil plus magnesium hydroxide (Phillips’ Milk of Magnesia®, Bayer Healthcare LLC)

Osmotic
• Lactulose
• Sorbitol
• Polyethylene glycol with electrolytes (Golytely®, Braintree Laboratories, Inc.; Colyte®, Schwarz Pharma)
• Polyethylene glycol without electrolytes (Miralax®, Schering-Plough HealthCare Products, Inc.)

Soluble Fiber
• Polyethylene glycol with sodium (Miralax®, Schering-Plough, Inc.)
• Polyethylene glycol without electrolytes (Methylcellulose (Citrucel®, GlaxoSmithKline)

Opioid-Receptor Antagonist
• Methylnaltrexone (Relistor®, Pfizer, Inc.)
• Alvimopan (Entereg®)

Saline
• Magnesium citrate
• Magnesium hydroxide (Milk of Magnesia®, Bayer Healthcare LLC)

Stimulant
• Senna (Senokot®, Purdue Products LP; ExLax®, Novartis Consumer Health, Inc.)
• Bisacodyl (Dulcolax®, Boehringer Ingelheim Pharmaceuticals, Inc.; Correctol®, Schering-Plough, Inc.)

Surfactant
• Docusate sodium (Colace®, Purdue Pharma)
• Docusate calcium (Surfax®, Chattem, Inc.)

Figure 4. Oral Laxative Classes and Agents

When Ms. J returned one week later for treatment, she reported improved pain control. She was having bowel movements about every two days using senna plus docusate sodium three times daily, and she had used lactulose once daily. Ms. J reported increased abdominal comfort, improved appetite, and less anxiety about her bowel function. Given the contrasting gastrointestinal toxicities of the chemotherapeutic agents and opioids, her bowel regimen required ongoing titration. After receiving her second cycle of chemotherapy, Ms. J was advised to temporarily decrease her senna plus docusate sodium doses and to contact her clinician if she developed diarrhea.

Conclusion

OBD is a common yet often underappreciated complication of opioid therapy. Failure to identify risk and begin prophylaxis can result in the development of symptoms and risk for serious sequelae. Opioids are a mainstay in the treatment of severe cancer pain (Reville et al., 2009); therefore, nurses play a critical role in educating themselves and their patients about medication side effects, including the signs and symptoms of OBD. Although current recommendations for assessment and management of OBD focus on constipation, they may change with the expansion of agents that address OBD’s underlying pathophysiology. Nurses should understand and apply evidence-based guidelines when available to reduce the incidence and severity of OBD, optimize pain control, and enhance quality of life in patients with advanced cancer.

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References


